PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Study protocol for a 9-month randomised controlled trial assessing the effects of almonds vs. carbohydrate-rich snack foods on weight loss and weight maintenance
AUTHORS	Carter, Sharayah; Hill, Alison; Yandell, Catherine; Buckley, Jonathan; Tan, Sze-Yen; Rogers, Geraint; Childs, Jessie; Matheson, Mark; Lamb, Kate; Ward, Susan; Stanton, Tasha; Fraysse, Francois; Hills, Andrew; Coates, Alison

VERSION 1 – REVIEW

REVIEWER	Rachel Brown University of Otago New Zealand
REVIEW RETURNED	24-Jan-2020

GENERAL COMMENTS	This trial aims to assess whether including almonds or carbohydrate-rich snacks into a nut-free energy-restricted diet promotes weight loss over 3 months of energy restriction, and limits weight regain during 6 months of weight maintenance. This study has several novel features: assessing the inclusion of almonds vs. a carbohydrate-rick snack on both weight loss and weight regain; and the metagenomic analysis. It also measures a wide range of useful outcomes. A limitation is the short weight loss period, but the researchers have addressed the rationale for this. The findings of the study will need to be interpreted with this in mind. The randomised parallel design is appropriate for addressing the study question. The methods are robust, using standard methods and validated questionnaires. The manuscript is clearly written and provides a good level of detail. I have some minor points below. Introduction The introduction provides good background information and rational for the study. 1. Page 4, lines 13-14: This sentence appears incomplete, please clarify. Objectives 2. Page 5, lines 5-7: I wonder if the hypothesis here should not be compared to a ‘nut-free’ diet, but a ‘nut-free diet containing a carbohydrate-rich snack? Methods and analysis 3. It would be useful to provide some rationale for the age range chosen for this study.

	4. It would be useful to provide some rationale for the BMI range chosen for this study. Some research suggests that obese people may compensate differently to those who are overweight or a healthy weight. Have the researchers considered comparing responses of overweight and obese individuals? Will the sample size allow for this subgroup analysis? 5. Will PAL values be used to estimate energy requirements? 6. It would be useful to provide a table of the nutritional composition of the nuts and carbohydrate-rich snacks. 7. How were the 5000, 6300 or 7600 kJ amounts derived? What if someone has an estimated energy requirement in excess of 11,000 kJ? For example, someone for someone with an energy requirement of 13,000 kJ, an intake of 7600 kJ would be quite low compared to someone with an energy requirement of 11,000 kJ. 8. Will the weight maintenance phase account for the new body weight of each participant? i.e. will energy requirements be recalculated? 9. How will the sub-sample for those in the doubly-labelled water measurement be chosen? 10. Will participants be provided with dietary scales to weight their foods for the 4-day food recording period? 11. Why are t-tests going to be used to compare baseline characteristics of the groups? Such significant tests assess the probability that that observed baseline difference could have occurred by chance (rather than bias). However, we already know that any differences are caused by chance; therefore, hypothesis testing is superfluous. Suggest removing this analysis. 12. Is the sample size sufficient to assess an interaction between dietary treatment and weight loss on the various outcomes?

REVIEWER	Kevin C Maki Indiana University School of Public Health, USA and Midwest Biomedical Research, USA I have received research grants and/or consulting fees from ACH Foods, Almond Board of California, Egg Nutrition Center, Avocado Board, National Cattlemen's Beef Association, National Dairy Council, Alliance for Potato Research & Education, Kellogg's, General Mills, Pepsico, and Pharmanex.
REVIEW RETURNED	10-Feb-2020

GENERAL COMMENTS	This paper describes a protocol evaluating the effects of almond consumption, vs. consumption of carbohydrate-rich snack foods, incorporated into reduced calorie diets, on weight loss and weight maintenance. Other parameters to be measured include energy expenditure and appetite regulation; markers of cardiometabolic health, liver health, and inflammation; and effects on the gut microbiome. The study is quite ambitious in its plan to assess so many parameters, and it is not clear that the authors have appropriately planned their statistical analyses to take into account the multiple comparisons. The authors have provided sufficient rationale for their study objectives, and, in general, the study

	design is appropriate. However, there are several areas in the paper where more details are needed, such as the description of data management and planned statistical analyses. The authors have provided a table showing the outcome measures planned at each visit (Table 1), a table listing the blood tests (Table 2), and a Figure representing the study design (Figure 1). However, I think a visual representation of all of the procedures at each of the clinic visits, i.e., weigh-ins, diet counseling, dispensing study products, etc. is also needed. It may be possible to incorporate this into Figure 1. Also, it seems as if there is a stronger emphasis on the blood measurements (Table 2) throughout the paper, which are tertiary objectives, and comparatively less emphasis on the primary and secondary objectives (body weight and body composition), and very little coverage of the fecal outcome analyses (also tertiary objectives). Please also see my specific comments below: Specific comments to Authors: 1. Abstract: suggest that you make it clear that the almonds and carbohydrate-rich snack foods will be provided, but that the rest of the subjects' diets will be self-selected, based on recommendations from dietitians. There is a statement about ethics in the abstract; I think a similar statement is needed somewhere in the body of the paper. 2. Introduction: 1st paragraph, line 8, instead of "positive impact" which might imply an increase in these parameters, suggest that you perhaps say "beneficial impact." 2nd paragraph, lines 39-43, the wording of this sentence is somewhat confusing. 2nd paragraph, lines 48-53, you have called out 1 cohort "EPIC-PANACEA", but it is not clear why you haven't simply included that in the prior sentence. Also, please check the journal guidelines regarding spelling out of acronyms/abbreviations. 2nd paragraph (page 4), line 13, I think you mean protective effect. 3. Objectives: Suggest that you provide rationale for the selection of 15% of energy from the almonds or the carbohydrate snacks. In each of the objective sections, suggest that instead of saying that you are evaluating the effects of almonds OR carbohydrate-rich snacks, that you say that you are evaluating the effects of almonds COMPARED TO carbohydrate-rich snacks. Line 5, page 5: spelling of hypothesize. 4. Study design: This section might be a good place to mention the ethics committee. 5. Participants: I recommend that you include the inclusion and exclusion criteria as a table, and provide more specific details of all of the inclusion/exclusion criteria. For example, later in the paper you mention that subjects completed palatability questionnaires to establish liking the test products, what were those criteria? What is the rationale for the lower BMI cutpoint of 27.5 kg/m2? Define "standard" drinks. 6. Randomisation, allocation concealment and sequence generation: I am not sure I agree with the statement "Decoding procedures will not be necessary during the study because the participants will know which foods they are consuming." While it is true that subjects will know what they are consuming, the staff conducting the assessments/analyses will be blinded. 7. Sample size calculation: Did you do any analyses to determine the number of subjects that would be required in order to detect differences for any of the secondary outcome variables? 8. Table 1: Is Fickiness Questionnaire supposed to be Pickiness Questionnaire? Are the Eysenck Personality Questionnaire and

	Brief Sensation Seeking Scale used for screening purposes only? If so, what scores are required on these for entry into the trial? Lp(a) is mentioned in the text of the paper, and in Table 2; I think it needs to be added to Table 1. In the text, VAP and NMR analyses are described, but this distinction is not made in Table 1. Please clarify. Also, will LDL particle size and concentration be measured with NMR? If so, please add to the table. 9. I think you need to provide rationale for using alpha-tocopherol (in plasma and urine) as a measure of compliance. 10. Study Intervention: Page 13, Line 3, I think you need to be clear that the 10 h fast is prior to every visit, not just the baseline visits. Page 13, Line 15, suggest say every 2 weeks, instead of "fortnightly." 11. Anthropometry: Page 13, Line 17, because you previously indicated that only nonpregnant people will be enrolled, you can delete this statement. 12. Biochemical measures: It should be stated that some of the analytes described in Table 2 will also be measured in urine (alpha-tocopherol, isoprostanes). 13. Table 2: the text indicates that alpha-tocopherol will also be measured in RBCs; this should be added to the table. The text suggests that NMR will also be used to measure lipoprotein particle concentrations and sizes; this should be clear in the table. 14. Appetite Regulation: Page 18, Line 24, have you considered using an indwelling catheter for collecting blood samples during the postprandial testing? 15. Accelerometry: Page 19, Line 47, you need to include an indication of which timepoint(s) during the trial the "14 consecutive days" refers to. (Same comment for the Doubly Labelled Water section where you say "over 14 days.") Page 21, Line 3, is this <4 valid days of accelerometry data throughout the whole trial, or for each measurement interval (i.e., 4 out of every 14 days)? 16. Dietary analysis: Page 22, this section should also include a description of the 24-h diet recalls that listed in Table 1. 17. Study Food Liking and Palpability Scores: Page 22, Line 50, does "alternative snack foods" refer to the carbohydrate-rich snacks? 18. Eating Behaviour, Mood and Personality: I question the need for including so many questionnaires about eating behavior mood and personality. 19. Quality of Life, Functional Mobility and Pain: I question the need for including these tests. 20. Fecal Microbiota: There has been an emphasis up to this point on the biochemical analyses. I would suggest that you expand the Blood testing table to include the fecal testing. Page 23, Line 55, since you say lowest responders, I think you should say highest responders, instead of "high responders." 21. Data Management: This section is rather brief. Will you be using case report forms to collect data? Will a database be created; how will data be entered? 22. Protocol Deviations: Please provide the definition for a protocol deviation; why is a letter to the editor of the journal necessary? 23. Adverse Events: More details are needed about how adverse events will be collected, and analyzed. 24. Statistical analysis plan: A more detailed description of the statistical analyses is necessary, particularly with regard to multiple comparisons. 25. Dissemination: It is not clear why there is mention of the test foods in the Dissemination section.

	26. Figure 1: Suggest including the screening visits on the study timeline also, and, as mentioned in a previous comment, I think it would be helpful to include more details about the study visit procedures (dispensing/collecting study products, weigh-ins, diet counseling, etc.) either in this figure or in a separate table. What do the numbers in each of the triangles and diamonds represent?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Rachel Brown
University of Otago
New Zealand

1. Page 4, lines 13-14: This sentence appears incomplete, please clarify.
Missing word at the end of the sentence, 'effect', now added.

Objectives
2. Page 5, lines 5-7: I wonder if the hypothesis here should not be compared to a 'nut-free' diet, but a 'nut-free diet containing a carbohydrate-rich snack?
Thank you for the suggestion. Change made.

Methods and analysis
3. It would be useful to provide some rationale for the age range chosen for this study.
Thank you for the suggestion.

Added, page 7: "Age range ensures physical maturity has been achieved and limits the possibility of chronic health conditions that would exclude the volunteer from participation."

4. It would be useful to provide some rationale for the BMI range chosen for this study. Some research suggests that obese people may compensate differently to those who are overweight or a healthy weight. Have the researchers considered comparing responses of overweight and obese individuals? Will the sample size allow for this subgroup analysis?

Thank you for the suggestion.

Added, page 7: "BMI range ensures sufficient weight available to lose and reduces the risk of chronic health conditions."

We do not have a specific hypothesis regarding the difference between overweight and obese individuals, so we do not intend to power the study to conduct this subgroup analysis. Also, the BMI range is narrow (i.e. BMI of 27.5-34.9kg/m2) and does not include the lower end of the overweight range (i.e. does not include 25- 27.5 kg/m2). Therefore it would not be appropriate to compare overweight and obese participants.

5. Will PAL values be used to estimate energy requirements?
Added, page 15: "Energy requirements will be determined by using the Schofield Equation, based on

age, sex, and baseline body weight, as well as self-reported physical activity captured via the International Physical Activity Questionnaire (IPAQ) to determine physical activity level (PAL)"

6. It would be useful to provide a table of the nutritional composition of the nuts and carbohydrate-rich snacks.
Thank you for the suggestion. See below (table included on page 15).

Table 3. Macronutrient Composition of Test Foods

Per 100g	Almonds	Weight Watchers Apple Crumble Bar	Rice Crackers
Energy (kJ)	2385.0	1270.0	1646.6
Protein (g) (%)	19.7 (14.0)	4.4 (5.9)	9.4 (9.8)
Total fat (g) (%)	50.5 (78.3)	1.0 (2.9)	5.6 (12.5)
Saturated fat (g)	3.8	0.3	1.4
Polyunsaturated fat (g)	12.8	0.3	1.2
Monounsaturated fat (g)	30.7	0.3	2.6
Carbohydrate (g) (%)	5.4 (3.6)	55.7 (72.4)	74.6 (76.8)
Sugars (g)	5.2	27.5	1.7
Starch (g)	0.2	28.2	72.8
Fibre (g) (%)	10.9 (3.7)	14.7 (9.3)	1.8 (0.9)

7. How were the 5000, 6300 or 7600 kJ amounts derived? What if someone has an estimated energy requirement in excess of 11,000 kJ? For example, someone for someone with an energy requirement of 13,000 kJ, an intake of 7600 kJ would be quite low compared to someone with an energy requirement of 11,000 kJ.

Energy amounts chosen are commonly used in weight loss trials. However, plans can be adapted if more energy is required.

Added, page 15: "Weight loss plans will be adapted if energy requirements are substantially higher than 7600 kJ/day."

8. Will the weight maintenance phase account for the new body weight of each participant? i.e. will energy requirements be recalculated?

Energy will not be recalculated, instead additional energy will be recommended on a case-by-case basis to keep weight stable.

Please see page 15: “During the weight maintenance phase, participants will be encouraged to stabilise their weight by increasing their overall energy intake by ~120-180 kcal/day (~500-750 kJ/day), with additional adjustments as required through dietetic consultation.”

9. How will the sub-sample for those in the doubly-labelled water measurement be chosen?
Added, page 24: “Each participant will be asked if they would like to participate in doubly labelled water testing until the required number of participants is achieved.”

10. Will participants be provided with dietary scales to weight their foods for the 4-day food recording period?
Added, page 25: “If required, we will lend participants a set of kitchen food scales.”

11. Why are t-tests going to be used to compare baseline characteristics of the groups? Such significant tests assess the probability that that observed baseline difference could have occurred by chance (rather than bias). However, we already know that any differences are caused by chance; therefore, hypothesis testing is superfluous. Suggest removing this analysis.
Thank you for the suggestion. Removed.

12. Is the sample size sufficient to assess an interaction between dietary treatment and weight loss on the various outcomes?

Added, page 10: “The study is powered on the primary outcomes of weight loss and weight regain.”

It may not be powered to determine effects on the other outcomes. Effects on the other outcomes will be hypothesis-generating and may need to be evaluated separately as the primary outcome in other studies if there is some evidence of an effect.

Reviewer: 2
Kevin C Maki
Indiana University School of Public Health

Midwest Biomedical Research, USA

Specific comments to Authors:
1. Abstract: suggest that you make it clear that the almonds and carbohydrate-rich snack foods will be provided, but that the rest of the subjects’ diets will be self-selected, based on recommendations from dietitians.

Thank you for the suggestion. Added the following to the abstract:

“Study snack foods will be provided.”

“Food will be self-selected, based on recommendations from the study dietitian.”

There is a statement about ethics in the abstract; I think a similar statement is needed somewhere in the body of the paper.

Thank you for the suggestion. Added to page 29.

2. Introduction: 1st paragraph, line 8, instead of “positive impact” which might imply an increase in these parameters, suggest that you perhaps say “beneficial impact.”

Change made, thank you.

2nd paragraph, lines 39-43, the wording of this sentence is somewhat confusing.

Changed to: “Nevertheless, changes in body fat distribution and reductions in fat stored in the liver can improve metabolic outcomes independent of weight changes.”

2nd paragraph, lines 48-53, you have called out 1 cohort “EPIC-PANACEA”, but it is not clear why you haven’t simply included that in the prior sentence.

Changed, thank you.

Also, please check the journal guidelines regarding spelling out of acronyms/abbreviations.

Changed where necessary, thank you.

2nd paragraph (page 4), line 13, I think you mean protective effect.
Changed, thank you.

3. Objectives: Suggest that you provide rationale for the selection of 15% of energy from the almonds or the carbohydrate snacks.

Please see page 14: “It is expected that the minimum quantity of almonds required to contribute 15% of energy will be 30 g, which is consistent with dietary guidelines.”

Also, 15% of energy is in line with previous studies in this area.

In each of the objective sections, suggest that instead of saying that you are evaluating the effects of almonds OR carbohydrate-rich snacks, that you say that you are evaluating the effects of almonds COMPARED TO carbohydrate-rich snacks.

Changes made, thank you.

Line 5, page 5: spelling of hypothesize.

Thank you.

4. Study design: This section might be a good place to mention the ethics committee.
Thank you for the suggestion. Added to ethics/dissemination session as per journal requirements. (Page 29).

5. Participants: I recommend that you include the inclusion and exclusion criteria as a table, and provide more specific details of all of the inclusion/exclusion criteria. For example, later in the paper you mention that subjects completed palatability questionnaires to establish liking the test products, what were those criteria?

Thank you for the suggestion. Table created, now Table 1, page 7.

What is the rationale for the lower BMI cutpoint of 27.5 kg/m2?

Added, page 7: “BMI cutpoint of 27kg/m^2 ensures sufficient weight available to lose.”

Define “standard” drinks.
Added to new eligibility table, table 1: “1 standard drink = 100 ml wine, 285 ml beer, 30 ml spirit.”

6. Randomisation, allocation concealment and sequence generation: I am not sure I agree with the statement “Decoding procedures will not be necessary during the study because the participants will know which foods they are consuming.” While it is true that subjects will know what they are consuming, the staff conducting the assessments/analyses will be blinded.
Removed. Thank you.

7. Sample size calculation: Did you do any analyses to determine the number of subjects that would be required in order to detect differences for any of the secondary outcome variables?
Please see response to issue #12 raised by Reviewer 1.

8. Table 1: Is Fickiness Questionnaire supposed to be Pickiness Questionnaire?

Changed to Pickiness/Fickiness Questionnaire as per reference: Raudenbush B, Van Der Klaauw NJ & Frank RA (1995) The contribution of psychological and sensory factors to food preference patterns as measured by the Food Attitudes Survey (FAS). Appetite 25, 1-15.

Are the Eysenck Personality Questionnaire and Brief Sensation Seeking Scale used for screening purposes only?

No.

If so, what scores are required on these for entry into the trial?

N/A.

Lp(a) is mentioned in the text of the paper, and in Table 2; I think it needs to be added to Table 1.

Done. Thank you. (NB: Table 1 is now Table 2).

In the text, VAP and NMR analyses are described, but this distinction is not made in Table 1. Please clarify. Also, will LDL particle size and concentration be measured with NMR? If so, please add to the table.

VAP will measure cholesterol + subclasses (added to tables).

NMR measures LDL particle size and concentration (added to tables).

9. I think you need to provide rationale for using alpha-tocopherol (in plasma and urine) as a measure of compliance.
Thank you for the suggestion. Added the following to page 21 with references: “Compliance with long-term almond consumption can be confirmed by measuring alpha-tocopherol levels.”

We will be measuring in plasma only (urine comments removed).

10. Study Intervention: Page 13, Line 3, I think you need to be clear that the 10 h fast is prior to every visit, not just the baseline visits.

Fasting is for Day 1 and Day 2 only, outlined on page 16.

Page 13, Line 15, suggest say every 2 weeks, instead of “fortnightly.”

Change made. Thank you.

11. Anthropometry: Page 13, Line 17, because you previously indicated that only nonpregnant people will be enrolled, you can delete this statement.
Removed. Thank you.

12. Biochemical measures: It should be stated that some of the analytes described in Table 2 will also be measured in urine (alpha-tocopherol, isoprostanes).
Urine analysis will not occur, removed.

13. Table 2: the text indicates that alpha-tocopherol will also be measured in RBCs; this should be added to the table.

We will be measuring in plasma only.

The text suggests that NMR will also be used to measure lipoprotein particle concentrations and sizes; this should be clear in the table.

Done, thank you.

14. Appetite Regulation: Page 18, Line 24, have you considered using an indwelling catheter for collecting blood samples during the postprandial testing?
A cannula will be used. Please see comment on page 21: “Blood samples will be collected via a BD Nexiva™ cannula blood collection system by a trained phlebotomist.”

15. Accelerometry: Page 19, Line 47, you need to include an indication of which timepoint(s) during the trial the “14 consecutive days” refers to. (Same comment for the Doubly Labelled Water section where you say “over 14 days.”)

Thank you for the suggestion. Added timepoints, also alerted the reader to table 2 (specifies timepoints).

Page 21, Line 3, is this <4 valid days of accelerometry data throughout the whole trial, or for each measurement interval (i.e., 4 out of every 14 days)?
Thank you for the suggestion. Added timepoints and also alerted the reader to table 2.

16. Dietary analysis: Page 22, this section should also include a description of the 24-h diet recalls that listed in Table 1.
Thank you for the suggestion. Added, page 25: “Adherence to energy-restricted diets will be assessed using 3 x 24-hour dietary recalls (via phone, at random times) during the weight loss and weight maintenance phases.”

17. Study Food Liking and Palpability Scores: Page 22, Line 50, does “alternative snack foods” refer to the carbohydrate-rich snacks?

Changed, thank you.

18. Eating Behaviour, Mood and Personality: I question the need for including so many questionnaires about eating behavior mood and personality.

We are seeking to obtain a comprehensive assessment of these variables.

19. Quality of Life, Functional Mobility and Pain: I question the need for including these tests.

Weight loss is associated with improved quality of life and functional mobility and reduced pain. We are seeking to evaluate how these change during the course of the study and potential relationships among these variables and with other variables.

20. Fecal Microbiota: There has been an emphasis up to this point on the biochemical analyses. I would suggest that you expand the Blood testing table to include the fecal testing.

Done, thank you.

Page 23, Line 55, since you say lowest responders, I think you should say highest responders, instead of “high responders.”
Change made, thank you.

21. Data Management: This section is rather brief. Will you be using case report forms to collect data? Will a database be created; how will data be entered?
Added, page 28: “Paper case report forms will be used to collect data at all clinic visits. Data will be entered twice into two separate password-protected Excel data files. Before analysis, data will be compared between files to ensure it has been correctly recorded.”

22. Protocol Deviations: Please provide the definition for a protocol deviation; why is a letter to the editor of the journal necessary?

If the protocol is changed we are required to alert the ANZCTR and the journal.

Changed to, page 28: “Deviations from the proposed protocol will be communicated via an update of the Australian and New Zealand Clinical Trial Registry and also through a letter to the editor of this journal.”

23. Adverse Events: More details are needed about how adverse events will be collected, and analyzed.
Added, page 28: “Adverse events will be recorded in the case report form. Adverse events that lead to withdrawals will be reported in future publications. We do not intend to formally analyse adverse events.”

24. Statistical analysis plan: A more detailed description of the statistical analyses is necessary, particularly with regard to multiple comparisons.

The study is powered on the primary outcomes of weight loss and weight maintenance.
We will analyse secondary outcomes without adjustment, but we will present unadjusted p-values & CIs for all pre-specified analyses (Perneger BMJ 1998) so readers can make adjustments (e.g., Bonferroni) at the level of Type I error control that they wish, at risk of making Type II errors.

25. Dissemination: It is not clear why there is mention of the test foods in the Dissemination section.
Removed, thank you.

26. Figure 1: Suggest including the screening visits on the study timeline also, and, as mentioned in a previous comment, I think it would be helpful to include more details about the study visit procedures (dispensing/collecting study products, weigh-ins, diet counselling etc.) either in this figure or in a separate table. What do the numbers in each of the triangles and diamonds represent?

Thank you for the suggestion. Changes as follows:

Removed numbers from diamonds. Added screening and pre-baseline visits. Added more detail to the key re. diet visits (testing information is available in the Outcome Measures table, table 2).

VERSION 2 – REVIEW

REVIEWER	Rachel Brown University of Otago, NZ
REVIEW RETURNED	22-Mar-2020

GENERAL COMMENTS	Thank you to the authors who have addressed all points from the review. Minor comment: Table 3: Suggest removing the decimal point for the energy values.

REVIEWER	Kevin C Maki Indiana University, USA I have received research grant support and/or consulting fees from: Acasti, Akcea, Amgen, AstraZeneca, Corvidia, Matinas BioPharma, Pharmavite, Sanofi Regeneron, Kellog, General Mills, 89BIO, Hass Avocado Board, American Egg Board, Beef Checkoff, Almond Board of California, National Dairy Council, American Potato Research & Education, and AlaskOmega.
REVIEW RETURNED	27-Mar-2020

GENERAL COMMENTS	Thank you for addressing my previous comments regarding your protocol paper. I think the paper is shaping up very nicely, but I do have a few additional suggestions, mostly minor, that I would like you to consider. Please see below: Specific comments to Authors: 1. The use of the abbreviation of AED for almond-enriched diet might be confused with its common use referring to automated external defibrillator. Could you perhaps just call it AD (almond diet), or perhaps AAD (almond-added diet)? 2. Page 4, lines 8-9: “suggests” should be “suggest,” because data is a plural word. 3. Page 7, Lines 8-14: I suggest adding “This” at the beginning of each new sentence that you added. Lines 15-17, I think the word “are” is missing prior to “listed in table 1.” 4. Table 1: “to either experimental groups” should be “to either experimental group” 5. Page 10, Lines 10-12 and Page 31, Lines 9-10: please verify that this is the correct way to refer to unpublished data for this journal. Line 28: the term “one-off” may not be universally understood. Suggest replacing with “single.” 6. Table 2 (and elsewhere in the paper): In your response to my previous question “Is Fickiness Questionnaire supposed to be Pickiness Questionnaire?” you said that you had changed it to Pickiness/Fickiness Questionnaire, and cited a reference by Raudenbush et al. (1995). I looked at this paper, and they refer to the questionnaire as the Pickiness/Finickiness Questionnaire. Please correct the spelling throughout the paper. 7. Table 3: suggest that you describe the Almonds in the table as “Unsalted, Whole, Natural Almonds with Skin.” Also, suggest that you provide a brand name for the rice crackers, since you have done that for the Weight Watchers’ Apple Crumble Bar. Are these macronutrients taken from the product labels? Were PUFAs and MUFAs reported on the labels? 8. Page 16, Line 3: Suggest that you replace the dash after Day 2 with a comma to match how you have written Day 1. Line 7: suggest that you add “on both days” at the end of this sentence. 9. Page 16, Line 31: you have used 1st person “us” in this sentence, but the rest of the paper has been written without using 1st person. I would suggest revising this sentence accordingly. 10. In response to my previous question about which visits required fasting, you indicated that fasting is for Day 1 and Day 2 only. However, in the Biochemical Measures section (page 17) it says that fasting occurs at “Day 1 baseline, 3-month and 9-month appointments.” The Anthropometry section is also a bit confusing regarding fasting, because it says that body weight will be recorded following an overnight fast, and it is not clear whether this is only referring to the baseline measurements or also the end of treatment measurements? Thus, I think additional clarification is needed about which visits, and for which measurements, subjects will be fasted. Furthermore, should Line 45 mention both Day 1 and Day 2 baseline visits? Table 2 shows that some of the blood biochemical measures will be completed on Day 1 and others on Day 2. 11. Table 4: Because F2-isoprostranes are also measured in urine, I think the table title should include Urine. Also, the doubly-labeled water urine sampling could be added to this table. Please ensure that you have included all of the abbreviations in the footnote, e.g., DPP-IV, NMR, etc. are missing.

	12. Page 20, Line 5: I think serum lipid should be plural “lipids.” Also, in lines 15-20, you say “this assay” quantifies all of the subclasses, and I think this refers back to NMR. However, you had said earlier in this paragraph (and in Table 4) that the lipoprotein subclasses will be measured with VAP and that NMR will just be used for LDL particle number [concentration] and size. Thus, in my opinion, the descriptions of the VAP and NMR analyses are still not clear. 13. Page 21, Line 5: instead of saying that compliance “can be confirmed” suggest that you say “will be confirmed.” 14. Page 25, Line 5: since there are two baseline visits (Day 1 and Day 2), wherever you mention baseline, I think you should be specific about which Day(s) you mean. Line 50: because all subjects are required to weigh their food for the 4-day food records, I think you need to provide the kitchen food scales to everyone to ensure they are using the same type of scale and collecting data in the same manner. Therefore, I do not think the explanation of “If required, we will lend participants a set of kitchen food scales.” Is an accurate description. 15. Page 26, Lines 24-27: this is not a complete sentence. 16. Page 30, Line 34-37: the strengths and limitations listing on page 3 indicated that this was the 1st trial to assess whether inclusion of almonds vs. carbohydrate-rich snack foods in an otherwise nut-free diet would improve weight loss and weight regain. However, in this later section of the paper you have omitted the comparator of vs. carbohydrate-rich snack foods, which I think is important. 17. Figure 1: I think the parentheticals after Day 1 and Day 2 in the legend should say (Wk -1, Wk 12, and Wk 36) for Day 1 and (Wk 0, Wk 13, and Wk 37) for Day 2, instead of having all weeks listed for both days.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Rachel Brown
University of Otago
New Zealand

Minor comment:

Table 3: Suggest removing the decimal point for the energy values.

Done. Thank you.

Reviewer: 2
Kevin C Maki
Indiana University School of Public Health

Midwest Biomedical Research, USA

Specific comments to Authors:

1. The use of the abbreviation of AED for almond-enriched diet might be confused with its common use referring to automated external defibrillator. Could you perhaps just call it AD (almond diet), or perhaps AAD (almond-added diet)?

Thank you for this suggestion and although we do agree that this abbreviation is used to refer to 'automated external defibrillator' it is also a commonly used abbreviation in the almond literature and so for consistency we would prefer to leave this as AED. (NB: AED and NFD abbreviations were used in our ANZCTR).

Examples of papers using AED abbreviation:

1. Foster GD, Shantz KL, Vander Veur SS, et al. A randomized trial of the effects of an almond-enriched, hypocaloric diet in the treatment of obesity. Am J Clin Nutr. 2012;96(2):249–254. doi:10.3945/ajcn.112.037895
2. de Souza RGM, Gomes AC, de Castro IA, Mota JF. A baru almond-enriched diet reduces abdominal adiposity and improves high-density lipoprotein concentrations: a randomized, placebo-controlled trial. Nutrition. 2018;55-56:154–160. doi:10.1016/j.nut.2018.06.001
3. Coates, A.M.; Morgillo, S.; Yandell, C.; Scholey, A.; Buckley, J.D.; Dyer, K.A.; Hill, A.M. Effect of a 12-Week Almond-Enriched Diet on Biomarkers of Cognitive Performance, Mood, and Cardiometabolic Health in Older Overweight Adults. Nutrients 2020, 12, 1180. doi.org/10.3390/nu12041180
4. Abazarfard Z, Eslamian G, Salehi M, Keshavarzi S. A Randomized Controlled Trial of the Effects of an Almond-enriched, Hypocaloric Diet on Liver Function Tests in Overweight/Obese Women. Iran Red Crescent Med J. 2016;18(3):e23628. Published 2016 Mar 6. doi:10.5812/ircmj.23628
5. Dhillon, J., Tan, S., & Mattes, R. (2017). Effects of almond consumption on the post-lunch dip and long-term cognitive function in energy-restricted overweight and obese adults. British Journal of Nutrition, 117(3), 395-402. doi:10.1017/S0007114516004463.

2. Page 4, lines 8-9: "suggests" should be "suggest," because data is a plural word.

Change made. Thank you.

3. Page 7, Lines 8-14: I suggest adding "This" at the beginning of each new sentence that you added. Lines 15-17, I think the word "are" is missing prior to "listed in table 1."

Done. Thank you.

4. Table 1: "to either experimental groups" should be "to either experimental group"

Change made. Thank you.

5. Page 10, Lines 10-12 and Page 31, Lines 9-10: please verify that this is the correct way to refer to unpublished data for this journal.

It is, thank you.

Line 28: the term "one-off" may not be universally understood. Suggest replacing with "single."

Change made. Thank you.

6. Table 2 (and elsewhere in the paper): In your response to my previous question “Is Fickiness Questionnaire supposed to be Pickiness Questionnaire?” you said that you had changed it to Pickiness/Fickiness Questionnaire, and cited a reference by Raudenbush et al. (1995). I looked at this paper, and they refer to the questionnaire as the Pickiness/Finickiness Questionnaire. Please correct the spelling throughout the paper.

Thank you, correction made throughout.

7. Table 3: suggest that you describe the Almonds in the table as “Unsalted, Whole, Natural Almonds with Skin.” Also, suggest that you provide a brand name for the rice crackers, since you have done that for the Weight Watchers’ Apple Crumble Bar. Are these macronutrients taken from the product labels? Were PUFAs and MUFAs reported on the labels?

Almond details added. Thank you.

All foods were analysed using Foodworks software (National Food Nutrient Database AUSNUT 2011-13) and this has been added as a footnote to the table.

The rice crackers (generic) were analysed in Foodworks: Rice Crackers, White Rice, Other. Detail added to table.

8. Page 16, Line 3: Suggest that you replace the dash after Day 2 with a comma to match how you have written Day 1. Line 7: suggest that you add “on both days” at the end of this sentence.

Changes made. Thank you.

9. Page 16, Line 31: you have used 1st person “us” in this sentence, but the rest of the paper has been written without using 1st person. I would suggest revising this sentence accordingly.

Change made. Thank you.

10. In response to my previous question about which visits required fasting, you indicated that fasting is for Day 1 and Day 2 only. However, in the Biochemical Measures section (page 17) it says that fasting occurs at “Day 1 baseline, 3-month and 9-month appointments.” The Anthropometry section is also a bit confusing regarding fasting, because it says that body weight will be recorded following an overnight fast, and it is not clear whether this is only referring to the baseline measurements or also the end of treatment measurements? Thus, I think additional clarification is needed about which visits, and for which measurements, subjects will be fasted. Furthermore, should Line 45 mention both Day 1 and Day 2 baseline visits? Table 2 shows that some of the blood biochemical measures will be completed on Day 1 and others on Day 2.

Yes. Day 1 and Day 2 appointments occur at baseline and at 3 months (Day 1 at week 12, Day 2 at week 13) and at 9 months (Day 1 at week 36 and Day 2 at week 37) as outlined in table 2.

Further clarification has been added to all outcome measures.

11. Table 4: Because F2-isoprostranes are also measured in urine, I think the table title should include Urine. Also, the doubly-labeled water urine sampling could be added to this table. Please ensure that you have included all of the abbreviations in the footnote, e.g., DPP-IV, NMR, etc. are missing.

Changes made. Thank you.

12. Page 20, Line 5: I think serum lipid should be plural “lipids.” Also, in lines 15-20, you say “this assay” quantifies all of the subclasses, and I think this refers back to NMR. However, you had said earlier in this paragraph (and in Table 4) that the lipoprotein subclasses will be measured with VAP and that NMR will just be used for LDL particle number [concentration] and size. Thus, in my opinion, the descriptions of the VAP and NMR analyses are still not clear.

Changed ‘lipid’ to ‘lipids.’ Changed ‘this assay’ to ‘VAP II’

13. Page 21, Line 5: instead of saying that compliance “can be confirmed” suggest that you say “will be confirmed.”

Done.

14. Page 25, Line 5: since there are two baseline visits (Day 1 and Day 2), wherever you mention baseline, I think you should be specific about which Day(s) you mean.

Done.

Line 50: because all subjects are required to weigh their food for the 4-day food records, I think you need to provide the kitchen food scales to everyone to ensure they are using the same type of scale and collecting data in the same manner. Therefore, I do not think the explanation of “If required, we will lend participants a set of kitchen food scales.” Is an accurate description.

Unfortunately this is what we planned for and what we are currently doing. The variation in scales between participants may introduce some error, but an individual participant will use the same scales throughout the intervention.

15. Page 26, Lines 24-27: this is not a complete sentence.

Edited.

16. Page 30, Line 34-37: the strengths and limitations listing on page 3 indicated that this was the 1st trial to assess whether inclusion of almonds vs. carbohydrate-rich snack foods in an otherwise nut-free diet would improve weight loss and weight regain. However, in this later section of the paper you have omitted the comparator of vs. carbohydrate-rich snack foods, which I think is important.

Added. Thank you.

17. Figure 1: I think the parentheticals after Day 1 and Day 2 in the legend should say (Wk -1, Wk 12, and Wk 36) for Day 1 and (Wk 0, Wk 13, and Wk 37) for Day 2, instead of having all weeks listed for both days.

Done. Thank you.

VERSION 3 – REVIEW

REVIEWER	Kevin C. Maki Indiana University and Midwest Biomedical Research, United States I have previously received research funding from Almond Board of California.
REVIEW RETURNED	26-May-2020 Thank you for your thorough and thoughtful responses to my previous comments and suggested revisions.